

Extracorporeal shock wave therapy induces degeneration and subsequent regeneration of nerve fibers innervating from DRG neurons in rat.

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Introduction:

Extracorporeal shock wave therapy (ESWT) has been applied to the management of various painful orthopaedic disorders. However, only a few reports have described the mechanism of the analgesic effect from this therapy. In this study, we investigated the analgesic effect of ESWT by immunohistological evaluation of dorsal root ganglion (DRG) neuron of rat.

Methods:

Activating transcription factor 3 (ATF3) is regarded as a marker of nerve injury, and growth-associated phosphoprotein (GAP43) is used as a marker of nerve regeneration. We examined ATF3 and GAP43 expression profiles in rat DRG neurons after ESWT.

Shock waves were applied to the skin of both hind paws in 28 rats, and 4 naive rats were used as controls. After 1, 2, 4, 7, 14, and 28 days, rats were sacrificed and the bilateral L4 and L5 DRGs were evaluated immunohistochemically.

Results:

The average number of ATF3-immunoreactive neurons significantly increased in the treated rats at each time point, and 77.0% of those neurons also exhibited immunoreactivity for GAP-43. Among the ATF3-immunoreactive neurons, 76.8% were large diameter cells (>30µm).

Discussion:

We showed that ESWT caused neuronal damage as represented by ATF3-immunoreactive neurons. Axonal regeneration was also confirmed by the expression of ATF3/GAP43 double-immunoreactive neurons. The significant increase in the number of ATF3-immunoreactive neurons observed after ESWT was sustained for at least 28 days. This result, however, does not assure the long-term analgesic effect of ESWT. The regeneration of nerve fibres which indicated by ATF3/GAP-43 double immunoreactivity began within 24 hours of ESWT, and 77.0% of ATF3-IR neurons were also reactive for GAP-43. This finding may relate to the temporary analgesic effect of ESWT in clinical subjects in whom repeated treatments are often necessary. With regard to the size distribution of ATF3-immunoreactive neurons, 23.2% were small and 76.8% were large, respectively. Large-diameter fibres from large neurons may be more sensitive to ESWT than small-diameter fibres from small neurons. The degeneration of nerve fibres originating from small ATF3-immunoreactive neurons may cause alleviation of pain because these fibres are mainly small-diameter fibres, which are involved in nociception and temperature perception. The degeneration of large-diameter fibres indicated by the expression of large ATF3-immunoreactive neurons may also relate to the analgesic effect of ESWT from the evidence that these fibres play a crucial role in some types of painful condition such as allodynia.